Complete Summary

GUIDELINE TITLE

Osteoarthritis of the knees.

BIBLIOGRAPHIC SOURCE(S)

Singapore Ministry of Health. Osteoarthritis of the knee. Singapore: Singapore Ministry of Health; 2007 May. 51 p. [91 references]

GUIDELINE STATUS

This is the current release of the guideline.

** REGULATORY ALERT **

FDA WARNING/REGULATORY ALERT

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory information has been released.

- April 7, 2005, Bextra (valdecoxib), Cox-2 inhibitors, Celebrex (celecoxib), Non-steroidal anti-inflammatory drugs (NSAIDS) (prescription and OTC, including ibuprofen and naproxen: Bextra (valdecoxib) withdrawn from the market and labels for other Cox-2 inhibitors and NSAIDS revised to include a boxed warning and a Medication Guide, highlighting the potential for increased risk of cardiovascular (CV) events and life-threatening gastrointestinal (GI) bleeding.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Osteoarthritis of the knees

GUIDELINE CATEGORY

Diagnosis
Management
Treatment

CLINICAL SPECIALTY

Family Practice
Internal Medicine
Orthopedic Surgery
Physical Medicine and Rehabilitation
Podiatry
Rheumatology
Surgery

INTENDED USERS

Advanced Practice Nurses
Nurses
Occupational Therapists
Physical Therapists
Physicians

GUIDELINE OBJECTIVE(S)

To provide guidelines for the diagnosis and treatment of osteoarthritis of the knees

TARGET POPULATION

Patients with osteoarthritis of the knees

INTERVENTIONS AND PRACTICES CONSIDERED

Diagnosis

1. History and physical examination, including palpation
2. Laboratory and radiological testing

Treatment/Management

1. Oral paracetamol
2. Non-selective non-steroidal anti-inflammatory drugs (NSAIDs)

3. Cyclo-oxygenase 2 (COX-2) selective inhibitors
4. Concomitant gastroprotective agents
5. NSAIDs with preferential cyclo-oxygenase 2 inhibition
6. Tramadol
7. Oral corticosteroids (not recommended)
8. Glucosamine/chondroitin
9. Viscosupplementation
10. Intra-articular (IA) corticosteroid
11. Topical non-steroidal anti-inflammatory drugs and capsaicin
12. Non-pharmacological management including exercise, weight reduction, hydrotherapy, transcutaneous electrical nerve stimulation (TENS), interferential current therapy, taping, braces and wedges, manual therapy, thermal therapy, ice therapy, and alternative therapies such as electro-acupuncture
13. Surgery

MAJOR OUTCOMES CONSIDERED

- Accuracy of diagnostic tests
- Symptoms (pain, stiffness, physical functioning)
- Muscle strength
- Range of motion
- Joint destruction

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Not stated

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Levels of Evidence

Level	Type of Evidence
1++	High quality meta-analyses, systematic reviews of randomised controlled trials (RCTs), or RCTs with a very low risk of bias.

Level	Type of Evidence
1+	Well conducted meta-analyses, systematic reviews of RCTs or RCTs with a low risk of bias
1-	Meta-analyses, systematic reviews of RCTs, or RCTs with a high risk of bias.
2++	High quality systematic reviews of case control or cohort studies. High quality case control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal.
2+	Well conducted case control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal.
2-	Case control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not causal.
3	Non-analytic studies (e.g. case reports, case series).
4	Expert opinion.

METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses
Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

These guidelines have been produced by a committee comprising rheumatologists, an orthopaedic surgeon, a family physician and a physiotherapist appointed by the Ministry of Health. They were developed using the best available current evidence and expert opinion.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Grades of Recommendation

Grade	Recommendation
A	At least one meta-analysis, systematic review of RCTs, or RCT rated as 1++ and directly applicable to the target population; or A body of evidence consisting principally of studies rated as 1+, directly applicable to the target population, and demonstrating overall consistency of results.
B	A body of evidence including studies rated as 2++, directly applicable to the target population, and demonstrating overall consistency of results; or Extrapolated evidence from studies rated as 1++ or 1+.

Grade	Recommendation
C	A body of evidence including studies rated as 2+, directly applicable to the target population and demonstrating overall consistency of results; or Extrapolated evidence from studies rated as 2++.
D	Evidence level 3 or 4; or Extrapolated evidence from studies rated as 2+.
GPP (good practice points)	Recommended best practice based on the clinical experience of the guideline development group.

COST ANALYSIS

Published cost analyses were reviewed in the preparation of this guideline. Cost-effectiveness issues are summarized in the "Major Recommendations" field as well as in the original guideline document.

METHOD OF GUIDELINE VALIDATION

Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Not stated

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Definitions of the grades of the recommendations (A, B, C, D, and Good Practice Point [GPP]) and level of the evidence (Level 1++, 1+, 1-, 2++, 2+, 2-, 3, 4) are presented at the end of the "Major Recommendations" field.

Diagnostic Approach to Joint Pain and Osteoarthritis

GPP - The diagnosis of osteoarthritis is made clinically based on history and physical examination, with laboratory and radiologic investigations selectively undertaken to exclude inflammatory arthritis, secondary osteoarthritis, and non-articular causes of joint pain. **(GPP)**

Analgesics in Osteoarthritis of the Knees

A - Paracetamol (acetaminophen) should be considered as the first line of treatment for relieving pain and improving physical functioning in osteoarthritis (Towheed et al., 2003; Jordan et al., 2003; Altman et al., 2000). **(Grade A, Level 1+)**

A - Non-selective non-steroidal anti-inflammatory drugs should be used for the acute relief of pain and improvement in function for as short a period as possible.

The benefits of using non-steroidal anti-inflammatory drugs should be weighed against the potential adverse reactions, especially with long-term use, in individuals at risk (Watson et al., 2000). (**Grade A, Level 1+**)

GPP - The selection of a non-steroidal anti-inflammatory drug for prescription for osteoarthritis knee should be based upon relative safety, patient acceptability and cost effectiveness. (**GPP**)

GPP - Patients who develop hypersensitivity reactions to non-selective non-steroidal anti-inflammatory drugs are usually able to tolerate cyclo-oxygenase 2 selective inhibitors. These should preferably be prescribed following demonstration of tolerance through supervised drug provocation tests. (**GPP)**

A - Patients with moderately high risk for gastroduodenal bleeds should receive concomitant gastroprotective agents (GPA) when using nonselective non-steroidal anti-inflammatory drugs (Gabriel, Jaakkimainen, & Bombadier, 1991).

Risk factors for gastrointestinal complications include (Gabriel, Jaakkimainen, & Bombadier, 1991):

- Age greater than 60 years
- Previous history of gastrointestinal events (e.g. peptic ulcer disease)
- Concomitant corticosteroid use

(Grade A, Level 1+)

A - Recommended prophylactic gastroprotective agents (GPA) against gastroduodenal ulcers include (Rostom et al., 2002):

- Standard dose of proton-pump inhibitors (omeprazole 20 mg once daily)
- Misoprostol 400-800 mcg/day
- Double dose of H2-receptor antagonists (famotidine 40 mg bd, ranitidine 300 mg bd)

(Grade A, Level 1+)

A - Cyclo-oxygenase 2 selective inhibitors may be used acutely in the reduction of pain from osteoarthritis of the knees (Bombardier et al., 2000; Silverstein et al., 2000; Schnitzer et al., 2004). Although these drugs have relatively lower risk of gastroduodenal adverse effects, long-term use has been associated with myocardial and cerebral infarction (Bresalier et al., 2005; Solomon et al., 2005; Nussmeier et al., 2005). (**Grade A, Level 1+**)

GPP - When non-steroidal anti-inflammatory drugs (including both cyclooxygenase 2 selective and non-selective non-steroidal anti-inflammatory drugs) are needed for the management of an individual patient, they should be prescribed at the lowest effective dose. The duration of treatment should be periodically reviewed and kept as short as possible. (**GPP**)

GPP - All non-steroidal anti-inflammatory drugs should not be prescribed in patients who have recently undergone coronary artery bypass graft (CABG) surgery and revascularization procedures. (**GPP**)

GPP - The benefits and risks of celecoxib and etoricoxib should be carefully assessed before they are prescribed to any individual patient, taking into consideration other available therapeutic options. (**GPP**)

GPP - Celecoxib or etoricoxib should not be prescribed for patients with established ischaemic heart disease, stroke or congestive heart failure. (**GPP**)

GPP - Caution should be exercised when prescribing celecoxib or etoricoxib to patients who have the following risk factors: hypertension, hyperlipidaemia, diabetes and smoking, as well as patients with peripheral arterial disease. (**GPP**)

GPP - Etoricoxib should not be prescribed for patients with hypertension whose blood pressure has not been adequately controlled. (**GPP**)

A - Meloxicam and nimesulide are two non-steroidal anti-inflammatory drugs with preferential cyclo-oxygenase 2 inhibition which may be used in the short term relief of pain from osteoarthritis of the knees (Bianchi & Broggini, 2003; Herrera & Gonzalez, 2003; Chang et al., 2001; Hawkey et al., 1998). (**Grade A, Level 1+**)

A- Tramadol may be used as an alternative to non-steroidal anti-inflammatory drugs for pain relief and improvement in physical functioning, especially where the risks of adverse effects from nonsteroidal anti-inflammatory drugs outweigh the benefits (Cepeda et al., 2006; Babul et al., 2004). (**Grade A, Level 1+**)

GPP - Oral corticosteroids are not indicated for management of knee osteoarthritis. (**GPP**)

Glucosamine/Chondroitin in the Treatment of Osteoarthritis

B - Patients who have failed to respond to analgesics and nonpharmacologic measures and want to try glucosamine may be given glucosamine sulphate 1500 mg once daily as pharmacologic studies suggest that maximal benefit is better achieved at this dose (Persiani et al., 2005). (**Grade B, Level 2++**)

B - Patients who are already taking glucosamine and report improvement in symptoms may discontinue after a period of 6 months as evidence suggests that regular use for more than 6 months is no more effective than placebo in the relief of joint pain (Cibere et al., 2004). (**Grade B, Level 1+**)

GPP - Patients allergic to shellfish should be warned about possible allergic reactions to glucosamine. (**GPP**)

Intra-articular Injections

B - Viscosupplementation can be used for treatment of osteoarthritis of the knee, where general measures or systemic therapies have failed or are contraindicated. It is effective with beneficial effects on pain, function and patient global

assessment; and at different post injection periods but especially at the 5 to 13 week post injection period when compared with placebo (Bellamy et al., 2006). (**Grade B, Level 1+**)

GPP - In Singapore, data on effectiveness are too limited to allow any conclusions to be drawn regarding cost-effectiveness of viscosupplementation. However, in view of the relative high cost of viscosupplementation and its comparable efficacy with other forms of systemic intervention, it should be considered only if general measures and systemic therapies have failed or are contraindicated. (**GPP**)

B - In patients with knee osteoarthritis who are symptomatic despite general measures and systemic therapies, evidence supports short term (up to two weeks) improvement of symptoms from intra-articular corticosteroid injection (Arroll & Goodyear-Smith, 2004). (**Grade B, Level 1**)

GPP - Regular use of intra-articular steroids is not recommended for osteoarthritis of the knees in the general practice setting. (**GPP**)

Topical Non-Steroidal Anti-inflammatory Drugs (NSAIDs) and Medications

A - Topical non-steroidal anti-inflammatory drugs (NSAIDs) can be considered for the short-term symptomatic relief of pain in osteoarthritis. Side effects of topical NSAIDs are usually minor. (**Grade A, Level 1+**)

A - Topical capsaicin may also be considered in relieving pain due to osteoarthritis. Transient local burning sensation may occur at the site of application. (**Grade A, Level 1+**)

Non-Pharmacological Management

A - Regular knee strengthening and aerobic exercises should be encouraged and taught to patients with osteoarthritis of the knees, as these improve functional ability, aerobic and endurance capacity and reduce knee pain. (**Grade A, Level 1+**)

A - Weight loss can result in significant changes in knee joint biomechanics with improved knee function for stair climbing and other daily activities. It is most effectively achieved by a combination of exercise and dietary control. (**Grade A, Level 1+**)

A - Regular water-based exercise or exercises in the pool are recommended as these exercises reduce pain and improve physical function in patients with osteoarthritis of the knees. (**Grade A, Level 1++**)

B - Transcutaneous electrical nerve stimulation, in the form of strong burst mode with high frequency, should be used to provide short-term relief of osteoarthritis of the knee pain, reduce stiffness and improve knee range of motion, with effects lasting for 4 weeks. (**Grade B, Level 1+**)

B - Interferential current may be used to reduce pain and increase in knee range of motion for osteoarthritis of the knee patients. (**Grade B, Level 1+**)

A - Taping may be used to shift the patella medially and provide effective relief of pain in osteoarthritis of the knee. (**Grade A, Level 1++**)

B - Lateral wedge insoles (tilt angle of 8.5 to 11 degrees) should be used to provide pain relief for osteoarthritis of the knee with medial osteoarthritis symptoms. (**Grade B, Level 1+**)

B - Valgus knee brace and knee sleeves may be used to provide significant improvement in functional tasks and unloading of varus deformity. (**Grade B, Level 1+**)

A - Manual therapy applied to the knee together with an exercise programme may be used to improve knee function and pain relief for patients with osteoarthritis of the knee. (**Grade A, Level 1+**)

A - Needle electro-acupuncture may be used as an adjunct for symptomatic relief of pain and improvement of knee function. (**Grade A, Level 1++**)

Surgery

GPP - A referral to the orthopaedic surgeon should be made when conservative management mentioned previously has failed. (**GPP**)

Cost-Effectiveness Issues

GPP - Pain medications are important in managing osteoarthritis symptoms and should be used concurrently with nutritional, physical, and educational interventions. Doctors should consider efficacy, adverse side effects, dosing frequency, and cost to the patient when recommending osteoarthritis treatments. (**GPP**)

C - For mild to moderate osteoarthritis pain, paracetamol is the drug of choice as it is cost-effective and has minimal side-effects. In treating moderate to severe osteoarthritis pain, the use of non-steroidal anti-inflammatory drugs and cyclo-oxygenase 2 specific inhibitors (for a patient who is at high risk of adverse upper gastrointestinal events) should be considered only if the patient is not responding to paracetamol (Kamath et al., 2003). (**Grade C, Level 2+**)

C - For patients who have failed medical therapy and who are suitable for surgical interventions, both unicompartmental and total knee arthroplasty are cost effective in terms of quality of life gain (Soohoo et al., 2006; Slover et al., 2006; Lavernia, Guzman, & Gachupin-Garcia, 1997). (**Grade C, Level 2+**)

Definitions:

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GPP (good practice points)	Recommended best practice based on the clinical experience of the guideline development group.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

REFERENCES SUPPORTING THE RECOMMENDATIONS

References open in a new window

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is specifically stated for each recommendation (see "Major Recommendations" field).

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

- Appropriate management of osteoarthritis of the knees
- Reduction in pain and improved physical functioning

POTENTIAL HARMS

Oral Paracetamol

Gastrointestinal discomfort was more frequent with non-steroidal anti-inflammatory drugs (NSAIDs) than with paracetamol.

Non-Selective NSAIDs

- Gastrointestinal (gastroduodenal perforations, ulcers and bleeds, small bowel perforations)
- Renal (hyperkalaemia, hypertension, oedema, acute renal insufficiency)
- Hypersensitivity reactions including periorbital angioedema, urticaria, rhinitis or attacks of asthma.

Emerging evidence suggests that there are cardiovascular risks associated with non-selective NSAIDs as well although this could not be conclusively demonstrated in a recent meta-analysis.

Cyclo-oxygenase 2 (COX-2) Selective Inhibitors

- Supervised drug provocation tests by specialists trained in allergy/immunology are recommended before using COX-2 inhibitors in NSAID-sensitive individuals.
- Although these drugs have relatively lower risk of gastroduodenal adverse effects, long-term use has been associated with myocardial and cerebral infarction.
- The COX-2 selective inhibitors have recently been found to be associated with increased cardiovascular events, leading to the withdrawal of rofecoxib in Singapore in October 2004.
- In addition to the increased cardiovascular risks, reports of severe cutaneous reactions (Stevens-Johnson syndrome, erythema multiforme, toxic epidermal necrolysis) among patients taking valdecoxib resulted in the drug being removed from the market in several countries including Singapore in April 2005.
- All non-steroidal anti-inflammatory drugs should not be prescribed in patients who have recently undergone coronary artery bypass graft (CABG) surgery and revascularization procedures.
- Celecoxib or etoricoxib should not be prescribed for patients with established ischaemic heart disease, stroke or congestive heart failure.

- Caution should be exercised when prescribing celecoxib or etoricoxib to patients who have the following risk factors: hypertension, hyperlipidaemia, diabetes and smoking, as well as patients with peripheral arterial disease.
- Etoricoxib should not be prescribed for patients with hypertension whose blood pressure has not been adequately controlled.

NSAID with preferential COX-2 inhibitors

Although it is indicated for the short-term relief of joint pain, there have been reports of elevated liver enzymes and hepatitis.

Tramadol

Nausea/giddiness

Glucosamine/Chondroitin

Patients allergic to shellfish should be warned about possible allergic reactions to glucosamine.

Viscosupplementation

Viscosupplements were comparable in efficacy to systemic forms of active intervention (e.g. NSAIDs), with more local reactions (post injection inflammation) but fewer systemic adverse events.

Topical NSAIDs and Medications

Topical capsaicin may cause local burning sensation and this may limit its use in some patients.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

- These guidelines are not intended to serve as a standard of medical care. Standards of medical care are determined on the basis of all clinical data available for an individual case and are subject to change as scientific knowledge advances and patterns of care evolve.
- The contents of this publication are guidelines to clinical practice, based on the best available evidence at the time of development. Adherence to these guidelines may not ensure a successful outcome in every case. These guidelines should neither be construed as including all proper methods of care, nor exclude other acceptable methods of care. Each physician is ultimately responsible for the management of his/her unique patient, in the light of the clinical data presented by the patient and the diagnostic and treatment options available.
- Some treatments which are widely available suffer from a paucity of good clinical evidence for efficacy and safety. These include the use of glucosamine, chondroitin and other nutraceutical products as well as

alternative therapies such as acupuncture and reflexology. However where data does exist, the workgroup has stated recommendations which hopefully will be beneficial to the clinician.
- Evidence-based clinical practice guidelines are only as current as the evidence that supports them. Users must keep in mind that new evidence could supercede recommendations in these guidelines.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

The following clinical quality indicators are proposed:

1. Knee pain and function should be assessed yearly.
2. Exercise in the form of a directed or supervised muscle strengthening or aerobic exercise program should have been prescribed at least once and reviewed at least once per year in ambulatory patients with no contraindication to exercise.
3. Weight should be measured yearly. Weight reduction should be advocated for patients with body mass index of >25 kg/m^2. Obese patients with body mass index >30 kg/m^2 should be referred to a medically-supervised weight reduction programme.
4. Activities of daily living should be assessed and physiotherapy assessment for assisted devices made should ADL be impaired.

IMPLEMENTATION TOOLS

Audit Criteria/Indicators
Personal Digital Assistant (PDA) Downloads
Quick Reference Guides/Physician Guides
Staff Training/Competency Material

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Living with Illness

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Singapore Ministry of Health. Osteoarthritis of the knee. Singapore: Singapore Ministry of Health; 2007 May. 51 p. [91 references]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2007 May

GUIDELINE DEVELOPER(S)

Singapore Ministry of Health - National Government Agency [Non-U.S.]

SOURCE(S) OF FUNDING

Singapore Ministry of Health

GUIDELINE COMMITTEE

Workgroup on Osteoarthritis of the Knee

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available from the Singapore Ministry of Health Web site.

Print copies: Available from the Singapore Ministry of Health, College of Medicine Building, Mezzanine Floor 16 College Rd, Singapore 169854.

AVAILABILITY OF COMPANION DOCUMENTS

The following is available:

- Osteoarthritis of the knees summary card. 2007 Apr. 8 p. Available in Portable Document Format (PDF) from the Singapore Ministry of Health Web site.

The following are also available:

- Audit criteria and a continuing medical education (CME) self-assessment are available in the original guideline document.
- The full text guideline and summary card are available for PDA download in ISilo and MSReader formats from the Singapore Ministry of Health Web site.

PATIENT RESOURCES

None available

NGC STATUS

This NGC summary was completed by ECRI Institute on October 29, 2007.

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